Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

PLAGL1 (pleomorphic adenoma gene-like 1)

Abbas Abdollahi

Sbarro Institute for Cancer Research and Molecular Medicine, College of Science and Technology, BioLife Sciences Building, Suite 446, Temple University, 1900 North 12th Street, Philadelphia, PA 19122, USA

Published in Atlas Database: August 2007

Online updated version: http://AtlasGeneticsOncology.org/Genes/PLAGL1ID41737ch6q24.html
DOI: 10.4267/2042/38498

Identity

Hugo: PLAGL1
Other names: DKFZp781P1017; LOT1; MGC126275; MGC126276; ZAC; ZAC1
Location: 6q24.2

DNA/RNA

Description

The genome is about 64 kbp with six exons and five introns. The major mRNA transcript is about 4.7 kb in size.

Transcription

At least three splicing variants (see figure).

Protein

Description

The PLAGL1 protein is a seven C2H2-type zinc finger protein. The seven zinc finger domain is located at the amino terminal region, from the amino acid residue 1 to 210. Additional features of note are proline and glutamine rich regions at the carboxyl terminal portion (residues 220 to 444). There are two nuclear localization signals at the amino terminal region.

Expression

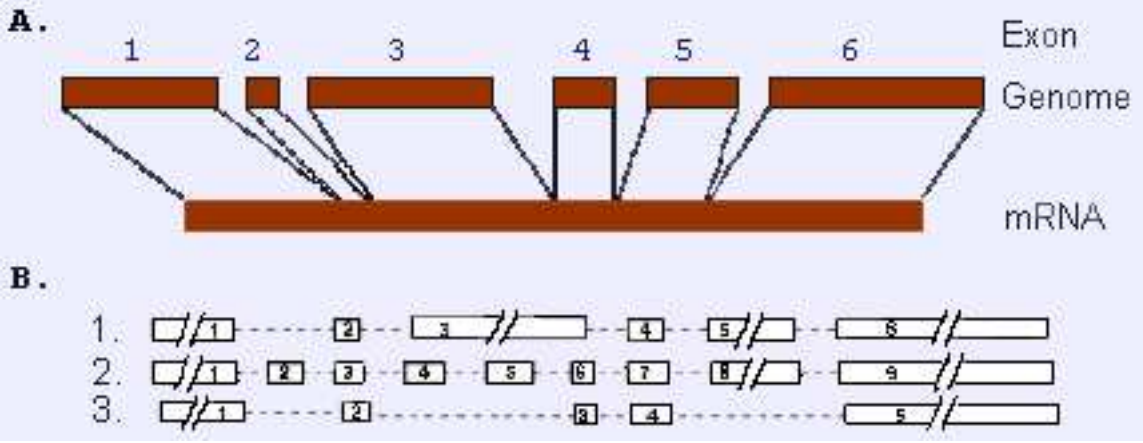
Ovary, breast, brain, liver, spleen, thymus, prostate, uterus, testis, intestine, colon, leukocytes.

Localisation

Nuclear.

Function

The PLAGL1 protein is a candidate tumor suppressor gene and has been shown to have transactivation and



Schematic view of the PLAGL1 gene. A. The six exons, shown in red, are 326; 72; 1443; 75; 475; 2380 bp, respectively. The introns are approximately 39; 2.6; 4.2; 12.5; 5.5 kbp in size, respectively. B. The figure shows three splice variants of PLAGL1; the exons are shown as a box.

Homology

Homologous to the mouse and Rat plagl1 and to the human PLAG1 and PLAGL2 proteins.

Mutations

Note: Mutation has not been found in the PLAGL1 coding region.

Implicated in

Carcinogenicity

Note: Alteration of the gene expression was found to be a potential genetic event silencing the PLAGL1 gene in cancers such as breast primary tumors, ovarian primary tumors and tumor-derived cell lines, basal cell carcinoma, head and neck squamous cell carcinoma (HNSCC), and extraskeletal myxoid chondrosarcoma (EMC). Several mechanisms have been shown to regulate the PLAGL1 gene expression, including growth factor receptor activation, epigenetic factors, maternal imprinting, and loss of heterozygosity (LOH). Allelic deletion of 6q24-q25, the PLAGL1 locus, in the tumor tissues has been shown in the cancers of ovarian, breast, HNSCC, and pheochromocytomas (PCCs).

Disease

Cancer

Transient neonatal diabetes (TNDM)

Note: Initial reports suggested that transient neonatal diabetes mellitus (TNDM), a rare condition characterized in the patients by intrauterine growth retardation, dehydration, failure to thrive, and hyperglycemia due to a lack of normal insulin secretion, is associated with paternal uniparental disomy (UPD) of chromosome 6 (UPD 6). Later studies showed the involvement of an imprinted gene in this disease within the chromosomal region 6q24.1-q24.3 between markers D6S1699 and D6S1010. Analysis of the CpG islands in the TNDM critical region, using DNA from TNDM patients with paternal UPD 6 and normal controls, suggested PLAGL1/LOT1/ZAC1 as a candidate imprinted gene for this disease.

Disease

Diabetes mellitus

To be noted

Note: PLAGL1 has been implicated in embryonic development. The gene is variably expressed in different tissues and stages during development. Inactivation of this maternally repressed gene resulted in intrauterine growth restriction, altered bone formation, and neonatal lethality.

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This article should be referenced as such:

Abdollahi A. PLAGL1 (pleomorphic adenoma gene-like 1). Atlas Genet Cytogenet Oncol Haematol.2008;12(2):127-129.